REMARKS

STATUS OF THE CLAIMS

Claims 1, 3-13 and 15-30 are pending in the application. Claims 2 and 14 are cancelled. Claims 15 and 19-29 have been withdrawn pursuant to a restriction requirement. Thus, Claims 1, 3-13 and 15-30 are presented for examination.

INFORMATION DISCLOSURE STATEMENTS

Applicant acknowledges with thanks the Examiner's review and consideration of the two previously submitted IDS's (January, 2004 and March, 2005).

WITHDRAWAL OF REJECTION UNDER **35 U.S.C. § 102(b)**

Applicant acknowledges with thanks the withdrawal of the rejection of Claims 1 and 4-9 under 35 U.S.C. § 102(b) based on Phan et al. (U.S. Patent No. 5,674,242) ("PHAN").

PROVISIONAL DOUBLE PATENTING REJECTION

In the current Office Action, the Examiner has rejected Claims 1, 3-13, 16-18 and 30 on the ground of provisional non-statutory obviousness-type double patenting on the basis of claims 1-23 of Strickler et al, U.S. Patent Application Serial No. 10/894,400 ("STRICKLER"); and claims 1 and 4-23 of Richard et al, U.S. Patent Application Serial No. 10/632,008 ("RICHARD I"), each individually.

In response to these provisional double patenting rejections, Applicants, through their attorney, respectfully traverse the provisional non-statutory obviousness-type double patenting rejection and its accompanying remarks. Applicants also respectfully state that the instant double patenting rejections will be addressed (1) if and when the "provisional" non-statutory obviousness-type double patenting rejection in each application is the only rejection remaining in that application; and/or (2) if and when the cited applications are issued as patents. See MPEP 804 I B:

> *If the "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection* and permit the application to issue as a patent, thereby converting the

"provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent.

Thus, since the co-pending applications have not issued as patents and the claims may be amended in the future, Applicants respectfully exercise their right to address the provisional rejections at a future date, particularly if and when the cited applications are issued as patents.

DOUBLE PATENTING REJECTION

In the current Office Action, the Examiner has rejected Claims 1, 3-13, 16-18 and 30 on the ground of non-statutory obviousness-type double patenting on the basis of claims 1-24 of Richard et al U.S. Patent No. 7,241,455 (formerly cited as U.S. Patent Application Serial No. 10/409,358 ("RICHARD II"). This was previously a provisional obviousness-type double patenting rejection. With the issuance of RICHARD II as a patent this now becomes an obviousness-type double patenting rejection. This rejection is respectfully traversed.

Claim 1 of RICHARD II provides for:

1. *An implantable or insertable medical device comprising (a) a therapeutic agent and (b) a polymeric release region that controls the release of said therapeutic agent upon administration to a patient, wherein said polymeric release region comprises* ***a radiation-crosslinked polymer that is crosslinked without a crosslinking agent****, wherein said radiation-crosslinked polymer is a radiation-crosslinked methylene-containing polymer that is formed from one or more hydrocarbon monomers and wherein said polymeric release region is crosslinked with a radiation dose of at least 10,000 rads.*

It is a basic tenet of chemistry that crosslinking builds molecular weight. In contrast to RICHARD II, the present invention teaches the opposite of crosslinking, and describes using radiation sensitive groups to reduce molecular weight in the polymeric release region.

Thus, the double patenting rejection should be withdrawn.

REJECTION UNDER **35 U.S.C. § 103(a) BASED ON PHAN IN VIEW OF CRUISE IN VIEW OF PINCHUK AND IN VIEW OF FURST**

The Examiner rejects Claims 1, 3-13, 16-18 and 30 under 35 U.S.C. § 103(a) based on PHAN, Cruise, U.S. Patent No. 6,537,569 ("CRUISE"), Pinchuk et al, U.S. Patent Application

Publication No. 2002/0107330 ("PINCHUK") and Furst, U.S. Patent Application Publication No. 2002/0099438 ("FURST"). This rejection is respectfully traversed.

The Examiner has not met her burden of establishing a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) ***must teach or suggest all the claimed features***. In addition, the teaching or suggestion to make the claimed combination and the reasonable expectation of success ***must both be found in the prior art, not in applicant's disclosure***. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The present invention contains a number of key concepts including:

1) using radiation sensitive groups to reduce molecular weight in the polymeric release region; and
2) treating the release region with a radiation dose of at least 100,000 rads that is effective to (i) reduce the molecular weight of the polymer and (ii) substantially increase the cumulative release of said therapeutic agent in an amount of at least 10% subsequent to administration to a patient.

None of the references alone or in combination teach or suggest the current invention.

PHAN teaches an endoprosthetic device carrying a polymer member having an embedded therapeutic compound. The polymer member is formed of a shape-memory polymer for expansion upon exposure to a selected stimulus. PHAN teaches the use of UV light to cause crosslinking in a mixture of monomers comprising methyl methacrylate, polyethyleneglycol methacrylate, butylemethacrylate in a 2:1.5:1 ratio with a crosslinker such as hexanedioldimethyacrylate and a thermal or UV initiator such as benzoin methyl ether or azobisisobutylnitrile (see col. 6, lines 21-64). Example 2 of PHAN describes the extrusion of a blend of polyocetenylene, polyethylene glycol and triallyl isocyanurate (crosslinking agent) with the extruded product then being crosslinked by exposure to irradiation in the form of a 2.5 Mrad electron beam.

In contrast to the present invention, PHAN:

1) uses radiation to provide crosslinking (with the associated increase in molecular weight);
2) adds crosslinking agents that will drive the reaction to effect such crosslinking with the effect of increasing molecular weight;
3) does not teach the polymers of the present invention;
4) fails to describe how to control the release of therapeutic agents in the face of PHAN's emphasis on driving the reaction to crosslinking; and
5) fails to describe how to select certain types of polymers (as currently claimed in the present invention) that would be useful to form polymeric release regions that would increase the cumulative release of said therapeutic agent.

The Examiner then turns to three other references to support this rejection.

The citation of CRUISE is completely without merit. CRUISE describes crosslinked hydrogels which have no relevance to PHAN or the present invention. As noted for PHAN, crosslinking teaches away from the present invention which is focused on reducing molecular weight and hydrogels are not taught or suggested by either PHAN or the present invention. The Examiner's position that the hydrogel subject matter does not make any difference is without merit. One skilled in the art would not look to hydrogel chemistry to modify technology that does not even mention hydrogels. CRUISE also does not teach irradiating a polymer to increase the cumulative release of the therapeutic agent from the device, or to have any impact whatsoever on the release kinetics of a therapeutic agent from a polymer, although it is well known in the hydrogel art that an increase in crosslinking decreases release rate.

The citation of PINCHUK is also not supportable or combinable with PHAN and/or CRUISE. As noted above, PHAN is directed to a shape memory polymer. PINCHUK's composition comprises: (a) a biocompatible block copolymer comprising one or more elastomeric blocks and one or more thermoplastic blocks and (b) a therapeutic agent, wherein the block copolymer is loaded with the therapeutic agent. PINCHUK uses specific blocks of selected polymer types to achieve a desired combination of hardness and elasticity. There is no teaching

or suggestion that the block copolymer compositions of PINCHUK could be used in PHAN or that the shape-memory polymers of PHAN could be used in PINCHUK

As noted in the previous response, it is critical to note that PINCHUK does not teach or even suggest the use of any radiation treatment for any purpose at all. In fact, the words "radiation," and "irradiate" do not even appear in the text of PINCHUK. The Examiner's attempt to combine a reference that does not even mention the use of any radiation treatment or the concept of crosslinking with a reference that uses radiation for crosslinking is without any foundation.

Additionally, PINCHUK merely describes therapeutic agents being released over time, while the present invention claims an increase in the release rate based on the treatment of the polymeric release region with radiation. Thus, one skilled in the art would not look to PINCHUK to combine with PHAN, and even if the references were combined, the present invention would not be achieved.

Also, any attempt to add CRUISE with its hydrogel technology to PHAN and/or PINCHUK must also fail. CRUISE uses only hydrogels and does not teach irradiating a polymer to increase the cumulative release of the therapeutic agent from the device. Indeed, as noted above, it is well known in the hydrogel art that an increase in crosslinking decreases release rate.

The final reference discussed by the Examiner is FURST. FURST describes a stent treated with gamma, beta and/or e-beam radiation to reduce the vascular narrowing of a stented section (paragraph 21). FURST also teaches the opposite of the present invention by using crosslinking (with the associated increase in molecular weight) to alter the release rate of biological agents (see paragraph 39). For example, FURST describes the crosslinking effect as partially or fully entrapping the salts of biological agents so that he agent takes a longer time to release see paragraph 39). This is a clear teaching away from the current invention. This exposure to crosslinking of a polymeric coating on a device such as a stent (but not the stent itself) is also described (paragraph 39).

While FURST indicates that the exposure to radiation alters the release of one or more vascular active agents or biological agents into the body passageway and that the release is controlled by the amount of crosslinking (paragraph 74), the amount of radiation used in FURST is less than 2000 rads (paragraph 39), which is orders of magnitude below the minimum amount

of 100,000 rads claimed in the present invention. Even the sterilization levels in FURST are described as less than 5000 rads (paragraph 41). It should also be noted that the 2000 rads is the upper limit of FURST and FURST even teaches away from the current invention by suggesting that lower amounts of radiation should be used (paragraph 39, last sentence).

Moreover, while the biocompatible coatings listed in FURST at paragraph 17 include some of the species listed in Claim 1, the complete failure of FURST to provide the radiation required to treat the polymer release region with with a radiation dose of at least 100,000 rads that is effective to (i) reduce the molecular weight of the polymer and (ii) substantially increase the cumulative release of said therapeutic agent in an amount of at least 10% subsequent to administration to a patient takes it outside of the invention.

Any attempt to combine FURST with any or all of PHAN, PINCHUK and CRUISE must also fail. FURST cannot be combined with PINCHUK which has no use or mention of radiation and requires a block copolymer containing an elastomeric block and a thermoplastic block. FURST is not useful with the hydrogel technology of CRUISE. Finally, FURST is not combinable with PHAN which requires a shape memory polymer.

Given the above remarks and the amendments to the claims, it is believed that the Examiner's rejection under 35 U.S.C § 103(a) has been obviated and withdrawal of this rejection is requested.

CONCLUSION

Applicants submit that Claims 1, 3-13 and 15-30 are in condition for allowance, early notification of which is earnestly solicited. Entry of this Amendment and Response is respectfully requested as it will put the case in a form for allowance or in better form for an appeal. It is believed that this Amendment and Response is being submitted in time for an Advisory Action should the Examiner require further changes to the Claims.

Should the Examiner be of the view that an interview would expedite consideration of this Response or of the application at large, the Examiner is requested to telephone the Applicant's attorney at the number listed below in order to resolve any outstanding issues in this case.

Respectfully submitted,

/Rosemary M. Miano/
Rosemary Miano
Registration No. 29, 674

Attorney for Applicant
Mayer & Williams, PC
251 North Avenue West, 2nd Floor
Westfield, NJ 07090
Tel.: 908-518-7700
Fax: 90-518-7795

Date: July 7, 2009